

Serial No.: 10/051,662**Our File No. 31140-B****REMARKS**

Applicants thank the Examiner for the interview of August 24, 2004. Applicant submits that the Vitamin D dosages in the higher Vitamin D dosages are not disclosed by Need under any reading of the Need reference. Furthermore, Need does not teach or motivate the use of Vitamin D plus progestin in regimens that are contraceptively effective. Thus, the specific claims having those limitations should be allowable over any interpretation of the Need reference.

However, Applicants submit that all the claims are allowable over the Need reference when read from the viewpoint of a person skilled in the art. Applicants submit the Declaration of Dr. Rodriguez on this point. As he explains, the Need reference does not disclose any data that would motivate a physician or any scientist to use or develop a composition comprised of a progestin and Vitamin D for any purpose. The Need data presented show no significant enhancement in bone mineral density in women on calcium who received progestin plus Vitamin D as compared to those who received progestin alone. In fact, the addition of Vitamin D appeared to somewhat abrogate the beneficial effect of the progestin. Thus, Need teaches away from the use of Vitamin D in combination with a progestin.

The bottom line from the viewpoint of a person skilled in the art is that given the data and teaching of Need, a reasonable physician or other scientist or practitioner would elect to not administer the progestin/Vitamin D combination, since the maximal effect would be achieved with progestin alone. There would be no need to add the Vitamin D compound with its potential side effects without any commensurate benefit to the patient.

A. Background of Applicants' Invention

The background of Applicants' invention is set forth in Dr. Rodriguez's declaration. That background sets forth a summary of Applicants' discovery that provided the

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motivation for the first time to combine Vitamin D and a progestin into a composition or a regimen to achieve a valuable benefit for women. The Need reference provides no motivation of resulting benefit, and actually teaches away.

B. From The Viewpoint Of A person Of Skill In The Art, The Need Reference Teaches Away From Applicants' Invention

The Need reference does not anticipate any of the pending claims. Applicants are not trying to claim the combination disclosed by Need. Thus, there is no rejection under 35 U.S.C. §102. Rather, the rejection is one of obviousness under 35 U.S.C. §103. However, in order to be held to be obvious using a single reference, there must be a motivation to modify the teachings of a reference to arrive at the claimed invention. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed.Cir.2000). However, neither the Need abstract nor the full Need reference provide any such motivation to arrive at the claimed subject matter here. Rather, Need teaches away.

The full Need reference shows that the study involved the administration of *separate* pills of various compound. Two of those compounds were a *separate pill* of progestin hormone and a *separate* pill of Vitamin D compound. Need administered the separate pills in various combinations to post-menopausal women with osteoporosis to determine if there was a benefit on osteoporosis from the various therapies, including some combination therapies. With respect to combining progestin and Vitamin D, Need found that there was absolutely no benefit as compared to progestin alone.

First, as stated in the Need abstract, Need combined (1) calcium with progestin and compared the results to (2) the combination of Vitamin D, calcium and a progestin hormone. The abstract of the Need reference states that there was no benefit to combining Vitamin D with progestin: "[c]alcium and ovarian hormones *with or without calcitriol*, caused a small non-

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significant rise in forearm mineral density.” In other words, one obtained the “small non-significant rise in forearm mineral density” by just combining calcium with progestin.

In fact, as shown in the full Need reference, the numerical gain in bone density for “calcium plus progestin” is slightly higher than “calcium plus vitamin D plus progestin,” although not significantly so:

There was a non-significant gain of bone in each of the two groups who received hormones together with calcium ($+4.4 \pm 5.2$ mg/ml/yr) or [calcium plus] calcitriol ($+3.9 \pm 6.4$ mg/ml/yr; Fig. 2).

(Need et al. at p. 277). This is shown graphically in Figure 2 where the “Ca+HORMONES” is slightly higher than “1,25+Ca+HORMONES.” As Dr. Rodriguez explains in his declaration, the Need data presented show no significant enhancement in bone mineral density in women on calcium who received progestin plus Vitamin D as compared to those who received progestin alone. In fact, the addition of Vitamin D appeared to somewhat abrogate the beneficial effect of the progestin (+ 4.4 mg/ml/yr forearm mineral density in women on progestin plus calcium, versus a lower bone density of +3.9 mg/ml/year forearm mineral density in women who received progestin plus calcium PLUS Vitamin D).

Thus, according to Dr. Rodriguez, Need teaches away from the use of Vitamin D in combination with a progestin. Given the data and teaching of Need, a reasonable physician or other scientist or practitioner would elect to not administer the progestin/Vitamin D combination, since the maximal effect would be achieved with progestin alone. There would be no need to add the potential side effects of the Vitamin D without any commensurate benefit to the patient.

C. Need Does Not Teach Or Motivate One to Arrive At Applicants' Claims

Claims 35-39, 41, and 49 recite Vitamin D and progestin in a single unit dosage.

The Need reference absolutely does not teach a *single unit dosage* containing a progestin and a

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Vitamin D compound as required by the claims. Thus, Need could only render these claims obvious if it provided some motivation to take the further, undisclosed step of combining a progestin and a Vitamin D compound into a single unit dosage. As Dr. Rodriguez states, because there was no benefit shown in the Need study from combining progestin and Vitamin D, there would be no motivation to combine the compounds for any purpose.

Applicants also submit that claims 45 and 46, from the second group of claims, are not obvious under the Need reference because the instant claims are drawn to compositions that are contraceptively effective. The combinations in the Need study were administered as hormone replacement therapies to post-menopausal, non-ovulating women whose average age was 61.5 and 65.7 with a SEM of +/-1.5-2.5 years. The combinations were being tested for their efficacy in increasing bone density for such women. Therefore, there would be no motivation from the teaching of making regimens with both Vitamin D and a progestin that are *contraceptively* effective.

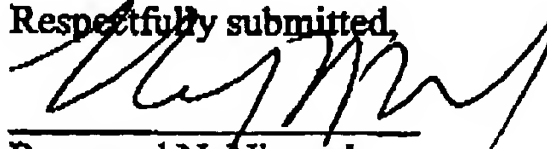
In addition, Applicants submit that there would be no motivation from Need to increase Vitamin D dosages if adding vitamin D did not provide an additional benefit over progestin alone. Thus, Applicants' claims with high dosages of Vitamin D are allowable.

Conclusion

Applicants request allowance of one or more of the claims pending in the Application.

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Respectfully submitted,



Raymond N. Nimrod
Reg. No. 31,987
606 Sunset Lane
Glencoe, IL 60022
(312) 927-5833

Serial No.: 10/051,662**Our File No. 31140-B****CERTIFICATE OF FACSIMILE**

I certify that this document and the attached Declaration of Dr. Rodriguez are being facsimile transmitted to the United States Patent and Trademark Office (Fax No. (571) 273-0571) on September 1, 2004.

Dated: September 1, 2004


Raymond N. Nimrod